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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/090,049

02/28/2002

Frank P. Luyten

NIH133.ICP1C2

6917

45311

7590

03/25/2005

KNOBBE, MARTENS, OLSON & BEAR, LLP  
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EXAMINER

ROMEO, DAVID S

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 03/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/090,049

Applicant(s)

LUYTEN ET AL.

Examiner

David S. Romeo

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 December 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 19 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 0202.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

**DETAILED ACTION**

The amendment filed 12/27/2004 has been entered. Claim 19 is pending.

Applicant's election of group IV, claim 19, drawn to a method inducing bone growth, and the species SEQ ID NO: 4 in the reply filed on 12/27/2004 is acknowledged. Because applicant  
5 did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim 19 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/27/2004.

10

***Claim Rejections - 35 USC § 112***

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of modulating Wnt activity by SEQ ID NO: 4, does not reasonably provide enablement for a method of treating a bone disorder with a bone-inducing  
15 amount of SEQ ID NO: 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The present specification discloses that Frzb in the *Xenopus* embryo experiments induces formation of secondary body axes which contain neural and muscle tissue (Examples 9-11, pages  
20 19-21). Frzb is capable of modulating Wnt activity (page 8, full paragraph 3). Frzb is contemplated for use in the therapeutic induction and maintenance of bone (paragraph bridging pages 9-10).

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The present claims are directed to or encompass the treatment of a bone growth disorder with Frzb. However, the prior art recognizes that many cytokines that subserve familiar functions postnatally play different or unknown roles embryologically and given the amino acid sequence of a cytokine and any of its actions one cannot predict when or where it will do what else. See

5 Nathan (37, cited by Applicants), page 981, paragraph bridging columns 1-2. All the work done on tissue induction by Frzb in the present application was done in *Xenopus* embryos. There are no working examples of bone tissue induction post natally by Frzb. The examiner is aware that the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of

10 experimentation. Lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art. Furthermore, Westendorf teaches that the Wnt signaling pathway promotes postnatal bone accrual and that Wnt antagonists impair osteoblast function and block bone formation (Abstract). Thus, Frzb would block bone formation rather than induce bone formation, as claimed. The present specification lacks

15 guidance for, and working examples of, inducing bone with Wnt antagonists. In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, and the unpredictability in the art, it would require undue experimentation for the skilled artisan to use the full scope of the claimed invention.

20

***Priority***

Applicants are claiming the benefit of U. S. Application Nos. 08/822,333 and 08/729,452, according to the preliminary amendment filed 02/28/2002. The benefit claim to U. S.

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Application Nos. 08/822,333 and 08/729,452 is not in compliance with the relevant statute and patent regulations, and is not accepted by the United States Patent and Trademark Office (Office). 35 U.S.C. § 120 is the provision of the patent code that allows for benefit claims to nonprovisional applications. Benefit claims under 35 U.S.C. § 120 must include a specific  
5 reference to the earlier filed (nonprovisional) application for which a benefit is sought. A "specific reference" requires: (1) the identification of the prior (nonprovisional) application by application number; and (2) an indication of the relationship between the nonprovisional applications, except for the benefit claim to the prior application in a continued prosecution application (CPA). The relationship between any two nonprovisional applications will be an  
10 indication that the later-filed nonprovisional application is either a continuation, divisional, or continuation-in-part of the prior-filed nonprovisional application. When there are benefit claims to multiple prior nonprovisional applications (e.g., a string of prior nonprovisional applications), the relationship must include an identification of each nonprovisional application as either a continuation, divisional, or continuation-in-part application of a specific prior nonprovisional  
15 application for which a benefit is claimed. The identification is needed in order to be able to verify if copendency exists throughout the entire chain of prior nonprovisional applications.

The OG Notice of 18 March 2003 clarifies how benefit claims under 35 U.S.C. 119(e), 120, 121 and 365(c) must be presented in applications in order to be in compliance with the relevant statute and patent regulations, and accepted by the United States Patent and Trademark  
20 Office.

Correction is required.

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### Drawings

The replacement drawings were received on 12/27/2004. These drawings are acceptable.

### Conclusion

5 No claims are allowable.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. De Robertis (U. S. Patent No. 6133232, cited by Applicants) discloses a protein that is identical to the presently disclosed SEQ ID NO: 4, as indicated below (Qy = SEQ ID NO: 4)(Db = De Robertis's protein):

10 GenCore version 5.1.6  
Copyright (c) 1993 - 2005 Compugen Ltd.

15 OM protein - protein search, using sw model  
Run on: January 10, 2005, 11:34:30 ; Search time 24.1486 Seconds  
(without alignments)  
892.530 Million cell updates/sec

20 Title: US-10-090-049-4  
Perfect score: 1738  
Sequence: 1 MVCGSPGGMLLLRAGLLALA.....SDSTQSQKSGRNSNPRQARN 325

25 Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5  
Searched: 478139 seqs, 66318000 residues

30 Total number of hits satisfying chosen parameters: 478139  
Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

35 Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

40 Database : Issued\_Patents\_AA:\*  
1: /cgn2\_6/ptodata/1/iaa/5A\_COMB.pep:\*  
2: /cgn2\_6/ptodata/1/iaa/5B\_COMB.pep:\*  
3: /cgn2\_6/ptodata/1/iaa/6A\_COMB.pep:\*  
4: /cgn2\_6/ptodata/1/iaa/6B\_COMB.pep:\*  
5: /cgn2\_6/ptodata/1/iaa/PCTUS\_COMB.pep:\*  
45 6: /cgn2\_6/ptodata/1/iaa/backfiles1.pep:\*

US-08-878-474-9  
; Sequence 9, Application US/08878474  
; Patent No. 6133232  
; INFORMATION FOR SEQ ID NO: 9:

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; SEQUENCE CHARACTERISTICS:
;   LENGTH: 325 amino acids
;   TYPE: amino acid
;   TOPOLOGY: linear
;   MOLECULE TYPE: peptide
US-08-878-474-9

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Query Match 100.0%; Score 1738; DB 3; Length 325;  
Best Local Similarity 100.0%; Pred. No. 2.3e-175;  
Matches 325; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MVCGSPGGMLLLRAGLLALAALCLLRVPGARAAACEPVRIPLCKSLPWNMTKMPNHLHHS	60
Db	1	MVCGSPGGMLLLRAGLLALAALCLLRVPGARAAACEPVRIPLCKSLPWNMTKMPNHLHHS	60
Qy	61	TQANAILAI EQFEGLLGTHCSPDLLFFLCAMYAPICTIDFQHEPIKPKCSVCERARQGCE	120
Db	61	TQANAILAI EQFEGLLGTHCSPDLLFFLCAMYAPICTIDFQHEPIKPKCSVCERARQGCE	120
Qy	121	PILIKYRHSWPENLACEELPVYDRGVCISPEAIVTADGADFPMDSSNGNCRGASSERCKC	180
Db	121	PILIKYRHSWPENLACEELPVYDRGVCISPEAIVTADGADFPMDSSNGNCRGASSERCKC	180
Qy	181	KPIRATQKTYFRNNYNYVIRAKVKEIKTKCHDVTAVVEVKEILKSSLVNI PRDVTNLYTS	240
Db	181	KPIRATQKTYFRNNYNYVIRAKVKEIKTKCHDVTAVVEVKEILKSSLVNI PRDVTNLYTS	240
Qy	241	SGCLCPPLNVNEEYIIMGYEDEERSRLLLVEGSI AEKWKDRLGKKVKRWDMKLRHLGLSK	300
Db	241	SGCLCPPLNVNEEYIIMGYEDEERSRLLLVEGSI AEKWKDRLGKKVKRWDMKLRHLGLSK	300
Qy	301	SDSSNSDSTQSQKSGRNSNP RQARN	325
Db	301	SDSSNSDSTQSQKSGRNSNP RQARN	325

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

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FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

DAVID ROMEO  
PRIMARY EXAMINER  
ART UNIT 1647

DSR  
MARCH 16, 2005